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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,775	01/23/2002	Steven Mark Eker	SRI/4578-2	8753

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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,775	EKER ET AL.	
	Examiner	Art Unit	
	Shubo (Joe) Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,3-6,8-22 and 99-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-22 and 99-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/06 has been entered.

Claims 1, 3-6, 8-22 and 99-104 are currently pending and under consideration.

Specification

The specification is objected to because of the following:

The title of the invention is not descriptive. The elected invention is drawn to a method of evaluating metabolic pathways and culturing cells, whereas the title is merely directed to modeling reaction pathways. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

It seems that the phrase "111 transportable compound" (note the singular form of compound) on page 33, lines 5-6 should be "111 transportable compounds" (note the plural form of compound).

Appropriate correction is required.

Claim Rejections-35 USC § 112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6, 8-22 and 99-104 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claims 1, 12, and 99 are amended to recite a limitation "to identify a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products." Upon further consideration of the specification in relation to the new limitation introduced, it is determined that the term "end-products" per se is not new matter as the original specification introduces the term on page 10, etc. The term is described as the first aspect of the system model representing a set of compounds that are considered end products for survival of the cell as opposed to the second aspect of the model representing a set of compounds that are considered available from the environment that are referred to as "transportable compounds" and the third aspect of the model representing compounds that are always present in the cell. However, the specification does not provide adequate description for the concept of identifying "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products." While it is noted that the specification describes on page, e.g. 2 the concept of identifying a set of precursor

substrates and/or chemical reactions that are sufficient to produce a set of target compounds or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of target compounds, there is no indication in the specification that the term "end-products," which represents the first aspect of the model, and the term "target compounds" mean the same. Although the specification does not provide an explicit definition for the term "target compounds," the statement on page 5 that "[t]he target compounds can include a modified protein or proteins that are required for the cell behavior" indicates that the target compounds do not have to be an end product but rather can be a compound from the environment, e.g. the transportable compound. Thus, a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of target compounds, as disclosed in the specification, may be different from a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products, as now required in the amended claims. Therefore, all things considered, the introduced new limitation of identifying "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products" is deemed new matter.

Claims 1, 3-6, 8-22 and 99-104 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability of the prior art; (g) the breadth of the claims; and (h) the relative skill in the art. The factors are analyzed in turn for the instant case as follows:

(a) In the instant case, the amount of experimentation required by a skilled artisan in order to practice of modeling metabolic pathways and culturing cells based upon the results thereof would require an unpredictable amount of experimentation for the following reasons:

(b) The claims are drawn to a method for evaluating at least one metabolic pathway using symbolic modeling and culturing cells in medium selected based upon identification of "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products." As set forth above, the specification does not provide adequate description for the identification of "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products and thus fails to provide guidance that teaches the skilled artisan how to evaluate metabolic pathways using symbolic modeling to identify "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical

reactions that are insufficient to produce the set of end-products." The specification also fails to provide guidance by which to select a medium for culturing cells based on the identification of "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products."

(c) The instant application does not present any working examples wherein metabolic pathways are evaluated using symbolic modeling to identify "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products," and a cell culture medium is selected based upon the results thereof.

(d)-(f) The nature of the invention, i.e. evaluating metabolic pathways using symbolic modeling to identify "a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products," selecting cell culture medium based upon the results of the identification, and culturing cells in the medium selected, is complex. While the prior art teaches of modeling metabolic pathways or genetic regulatory pathways in cells, such as those taught by Yuh et al. (IDS document: Science, Vol. 279, pages 1891-1902, 1998) for sea urchin genes, by Ouzounis et al. (IDS document: Genome Research, Vol.10, page 568-576, 2000) for the E. coli system, and by Weng et al. (IDS document: Science, Vol. 284, page 92-96, 1999) for general biological systems. As discussed by Weng et al., "[b]iological signaling pathways interact with one another to form complex network. Complexity arises from the

large number of components, many with isoforms that have partially overlapping functions; from the connections among components; and from the spatial relationship between components." See page 92. Weng et al. further state that although techniques in computations "are well developed in engineering contexts, we are not aware of any applications that approach the scale and complexity of the geometry and interactions in the cell. In addition to the purely numerical issues, it is a significant challenge to develop user interfaces that will enable experimental biologists who are not expert computer programmers to use such complex computational programs with relative ease." See page 95, middle and right columns. Furthermore, the prior art does not teach selecting cell culture medium based on the results of modeling of cellular metabolic pathways. Clearly, the prior art is unpredictable with regards to modeling of the complex biological systems and culturing cells in medium selected based on the results of the modeling.

(g)-(h) The claims, drawn to a method for evaluating metabolic pathways using symbolic modeling to identify a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products and culturing cells in a medium selected based upon the results of the identification, are extremely broad, especially considering the broad arrays of biological systems and the broad and complex metabolic pathways in such broad arrays of biological systems. The level of skill of those in the art who practice such as method of modeling metabolic pathways and culturing cells in a medium selected based upon the results of the identification is extremely high given the requirement of high skills in computations and bioinformatics and knowledge of the biological systems.

The skilled practitioner would first turn to the instant specification for guidance in practice of evaluating metabolic pathways using symbolic modeling to identify a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products and culturing cells in a medium selected based upon the results of the identification. However, the specification does not provide sufficient guidance of practicing the method as claimed. As such, the skilled practitioner would turn to the prior art for such guidance. However, the prior art does not teach the claimed method. Finally, said practitioner would turn to trial and error experimentation for evaluating metabolic pathways using symbolic modeling to identify a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products and culturing cells in a medium selected based upon the results of the identification without sufficient guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-6, 8-22 and 99-104 are rejected under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims, directly or indirectly, recite to identify a set of precursor substrates and/or chemical reactions that are sufficient to produce a set of end-products or a second

set of precursor substrates and/or chemical reactions that are insufficient to produce the set of end-products." The terms "sufficient" and "insufficient" are relative terms which render the claims indefinite. The terms are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Without a clear standard to ascertain the requisite degree of being "sufficient" or "insufficient," one of ordinary skill in the art would know what precursor substrates and/or chemical reactions are sufficient to produce a set of end-products or insufficient to produce the set of end-products.

Clarification of the metes and bounds of the claims is requested.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Shubo (Joe) Zhou, Ph.D.

Patent Examiner